**REMARKS**

Claims 25 and 28-35 presently appear in this case. No claims have been allowed. The present amendment supplements applicant's main response filed September 15, 2004, in response to the official action of April 15, 2004. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to an isolated amino-terminally truncated RANTES polypeptide having the sequence of residues 3-68 if the RANTES polypeptide of SEQ ID NO:1. The invention further relates to pharmaceutical compositions comprising such a truncated RANTES polypeptide and methods of use thereof.

The present amendment is intended to supplement applicant's amendment of September 15, 2004. It is respectfully requested that this supplemental amendment be admitted pursuant to 37 C.F.R. §1.111(a)(2), which became effective on October 21, 2004. The RCE filed in this case was filed on October 15, 2004, prior to the date when the new rules relating to supplemental amendments became effective. Thus, it was not then realized that, unless suspension was requested with the RCE, a supplemental amendment could not be filed absent compliance with 37 C.F.R. §1.111(a)(2). Accordingly, it is urged that the examiner exercise his discretionary authority to enter this supplemental amendment,

assuming that this supplemental amendment reaches the examiner in sufficient time to be entered into the application filed before the examiner considers the prior reply. In the explanatory notes accompanying the rule-making package of September 21, 2004, the following statement appears at 69 FR 56517 (2004):

> Examiners may enter and consider other supplemental amendments that are not listed in Section 1.111(a)(2)(i).

From this, it is clear that the examiner has the discretion to enter this response. Accordingly, this response should be entered because of the special situation that the RCE was filed prior to the effective date of the new rules, and it would therefore be unfair to apply them to the present supplemental amendment in the present case.

Furthermore, the present supplemental amendment should be entered in accordance with 37 C.F.R. §1.111(a)(2)(i)(C), (D) or (F). First, it is believed that the present amendment places the case into condition for allowance. Secondly, the amendment to claim 25 is being made in light of comments provided by the examiner in the advisory action of September 23, 2004, after the filing of applicant's amendment of September 15, 2004. Thirdly, it is believed that this amendment at the very least simplifies issues for appeal. Accordingly, consideration of the present supplemental

amendment in conjunction with applicant's amendment of September 15, 2004, is respectfully urged.

Following applicant's amendment of September 15, 2004, applicants received an advisory action advising applicants that the recitation of "CCR1 and CCR3 antagonistic activity" and "CCR5 agonistic activity" are new issues that have not been searched previously. The examiner further stated that applicants have failed to provide information as to where these specific limitations are in the instant specification.

Claim 25 has now been amended to delete specific reference to CCR1 and CCR3 RANTES antagonistic activity and CCR5 agonistic activity. Instead, the claim has been amended to read that the truncated RANTES polypeptide of the present invention "has the ability to inhibit monocyte cell chemotaxis towards CC chemokines", and "the ability to retain the capacity of intact RANTES to bind CCR5". As to the ability to inhibit monocyte cell chemotaxis towards CC chemokines, the examiner's attention is invited to page 18, Table IV, of the present specification, in conjunction with the paragraph bridging pages 13 and 14, and Table I at page 15. As to the ability to retain the capacity of intact RANTES to bind CCR5, reference is made to page 17, line 12, of the present specification.

While this definition of the properties of the truncated RANTES polypeptide of the present invention is slightly different from that submitted after the previous final rejection, the arguments relating to the references are still fully applicable. It is totally unexpected that the same compound will have the ability to inhibit monocyte cell chemotaxis towards CC chemokines, and yet will retain the capacity of intact RANTES to bind CCR5. This unusual combination of properties is not suggested by Gong or Rollins. There certainly would have been no reasonable expectation from any reading of Gong that RANTES(3-68) will have the ability to inhibit monocyte cell chemotaxis towards CC chemokines, but will retain the capacity of intact RANTES to bind CCR5. Maintenance of CCR5 binding, and the agonistic properties with respect thereto, are totally surprising, and would rebut any *prima facie* case of obviousness established by the examiner. Furthermore, the Noso reference of record would cause one of ordinary skill in the art to believe (erroneously) that the 1-2 truncation of RANTES would be fully agonistic. Therefore, there would have been no reasonable expectation from a reading of Gong and Noso that the 1-2 truncation would inhibit monocyte cell chemotaxis towards CC chemokines, yet would retain the capacity of intact RANTES to bind CCR5. The combination of Rollins with Proudfoot does not establish a

*prima facie* case of obviousness for the same reasons as discussed above with respect to Gong. The special properties of the now claimed single embodiment, RANTES(3-68), would not have been reasonably predictable to one of ordinary skill in the art, and would not have been expected.

Accordingly, for the reasons presented in applicant's amendment of September 15, 2004, as supplemented above, the examiner has not established a *prima facie* case of obviousness, because those of ordinary skill in the art would not have had motivation to make the necessary changes with a reasonable expectation of success. However, even to the extent that it is considered that a *prima facie* case of obviousness has been established, or that there is *prima facie* structural obviousness, such has been rebutted by the evidence of unexpected properties that the specification establishes for the claimed truncated RANTES polypeptide. It is well established that the presence of an unexpected property is evidence of non-obviousness, even with respect to a chemical compound. In this regard, the examiner's attention is invited to MPEP 716.02(a)III, which states:

> **III. PRESENCE OF AN UNEXPECTED PROPERTY IS EVIDENCE OF NONOBVIOUSNESS**
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> Presence of a property not possessed by the prior art is evidence of nonobviousness. *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) (rejection of claims to compound structurally similar to the prior art

> compound was reversed because claimed compound unexpectedly possessed anti-inflammatory properties not possessed by the prior art compound); *Ex parte Thumm*, 132 USPQ 66 (Bd. App. 1961) (Appellant showed that the claimed range of ethylene diamine was effective for the purpose of producing " 'regenerated cellulose consisting substantially entirely of skin' " whereas the prior art warned "this compound has 'practically no effect.' "). The submission of evidence that a new product possesses unexpected properties does not necessarily require a conclusion that the claimed invention is nonobvious. *In re Payne*, 606 F.2d 303, 203 USPQ 245 (CCPA 1979). See the discussion of latent properties and additional advantages in MPEP § 2145.

The examiner's attention is also invited to MPEP 2144.09, and particularly in the section titled "*Prima Facie* Case Rebuttable by Evidence of Superior or Unexpected Results", which states, in pertinent part:

> A *prima facie* case of obviousness based on structural similarity is rebuttable by proof that the claimed compounds possess unexpectedly advantageous or superior properties. *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) (Affidavit evidence which showed that claimed triethylated compounds possessed anti-inflammatory activity whereas prior art trimethylated compounds did not was sufficient to overcome obviousness rejection based on the homologous relationship between the prior art and claimed compounds.); *In re Wiechert*, 370 F.2d 927, 152 USPQ 247 (CCPA 1967) (a 7-fold improvement of activity over the prior art held sufficient to rebut *prima facie* obviousness based on close structural similarity).

Accordingly, for the reasons submitted herein, in conjunction with the reasons submitted in applicant's amendment of September 15, 2004, all of the claims now present in case clearly define over the references of record and fully comply with 35 U.S.C. §112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this **Supplemental Amendment** is being facsimile transmitted to the Patent and Trademark Office, on the date shown below.

Jonathan Brammer
Name

_____
Signature

December 21, 2004
Date